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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,548	10/18/2001	Dongfang Liu	M0656/7070(HCL)	7782

23628 7590 02/25/2005

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EXAMINER	
MCINTOSH III, TRAVISS C	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,548	LIU ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *4,13,33-35,127-129,135-139,164-167,200-202,208-213,217,218 and 220-222* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-38,42,43,58,59,73,79,82,89-91,99,113-140,158-170,176,177 and 184-222.

Continuation of Disposition of Claims: Claims rejected are 1-3,5-12,14-32,36-38,42,43,58,59,73,79,82,89-91,99,113-126,130-134,140,158-163,168-170,176,177,184-199,203-207,214-216 and 219.

DETAILED ACTION

The Amendment filed December 8, 2004 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1, 17, 24-25, 27-31, 38, 42-43, 58-59, 73, 79, 91, 113-122, 124-125, 130-134, 158-161, and 196 have been amended.

Claims 141-157, 171-175, and 178-183 have been canceled.

Claims 204-222 have been added.

Remarks drawn to rejections of Office Action mailed June 4, 2004 include:

Specification objection: which has been maintained for reasons of record.

Claim objections: which have been overcome by applicant's amendments and have been withdrawn.

112 1st paragraph rejections: which have been maintained in part for reasons of record.

112 2nd paragraph rejections: which have been maintained on part for reasons of record.

102(b) rejection: which has been maintained for reasons of record.

103(a) rejection: which has been overcome by applicant's arguments and has been withdrawn.

An action on the merits of claims 1-38, 42-43, 58-59, 73, 79, 82, 89-91, 99, 113-140, 158-170, 176-177, and 184-222 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). In the instant case, applicants state on page 50, lines 14-15 of the specification that "all references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference", however, applicant's are relying on various references to teach essential material, such as the biotechnology derived heparin of claim 6 and chemically modified heparin of claim 7 wherein the specification defines the same on page 21 as: "the term biotechnological heparin encompasses heparin that is prepared from natural sources of polysaccharides which have been chemically modified and is described in Razi et al., Bioche. J. 1995 Jul 15;309 (Pt 2): 465-72. Chemically modified heparin is described in Yates et al., Carbohydrate Res (1996) Nov 20;294:15-27, and is known to those of skill in the art. Synthetic heparin is well known to those of skill in the art and is described in Petitou, M. et al., Bioorg Med Chem Lett. (1999) Apr 19;9(8):1161-6 and Vlodavsky et al., Int. J. Cancer, 1999, 83:424-431".

Applicant's arguments filed December 8, 2004 have been fully considered but they are not persuasive. Applicants argue that "the references serve to demonstrate that the terms are well known to those of ordinary skill in the art as are the methods of making the compounds to which the terms refer" and that the "listing of these references in the specification is not for the purpose of incorporating essential material". However, as set forth supra, applicants state on page 50, lines 14-15 of the specification that "all references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference". Applicants are claiming various heparins, such as biotechnological heparin, and do not teach how to make the same, but rely on various publications to teach how to make these products, and thus are indeed attempting to incorporate essential material by reference. If applicants do not intend to incorporate anything by these references as they assert, then applicants should delete the phrase "all references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference" from the specification.

Claim Rejections - 35 USC § 112

The rejection of claims 6-10, 32, 121, 123, 162, 185, and 196 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. Newly added claims 214 and 216 are rejected for the same reasons. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims all comprise various "biotechnology derived heparin", "chemically modified heparin", "heparin analogue", "AT-III

binding saccharides", or "unfractionated heparin preparations". Applicants have not adequately described how to make these products, and have relied on various references which they improperly attempted to incorporate by reference to teach how to make said products. Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. ***In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973).***

Applicant's arguments filed December 8, 2004 have been fully considered but they are not persuasive. Applicants argue that the references are being cited to demonstrate the knowledge in the art at the time of the application, and that they are not cited to teach essential material. However, it is noted that if applicants are claiming "biotechnology derived heparin", for example, the examiner considers this essential material, and applicants have not taught how to make "biotechnology derived heparin", but rather they have pointed to non-patent literature to teach how to make the claimed products. Applicants should not teach how to find out how to make their claimed invention, but instead should teach how to make and use their claimed invention, as required by 112 1st paragraph, which they have not. Moreover, applicants remind the examiner that "possession merely requires that the claimed invention be described in such a way that the meaning of the terms would have been clear to one of ordinary skill in the art" and that since "these terms were known to those of ordinary skill in the art... the written description requirement is satisfied". However, this appears to be an argument to a 112 2nd paragraph rejection, not a 112 1st paragraph rejection. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g.,

Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); ***Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116***. Applicants could not have had possession of the claimed invention if they rely on various references to teach that which they are claiming.

Claims 5-9, 43, 58, 82, 89-90, 116-129, 135-140, 162, 185, 196-202, 214, 216, and 219-220 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation in a dependent claim of the source of an active agent to be used in a method from which said claim depends, wherein the "source of the active agent" does not result in a patentably distinguishable methodological and manipulative difference in how said active agent's source impacts the method from which it depends, renders the claim(s) in which it occurs and which depend therefrom indefinite for failing to distinctly articulate how such a recitation further limits the method from which said dependent claim(s) applicant regards as the invention. In the instant case, claim 6 provides that "wherein the heparin is a biotechnology derived heparin", and it is unclear how the method of making the heparin will effect the method of using the heparin, as the molecule heparin is heparin, regardless of where it comes from. Applicants argue that the claim is limiting, as claim 3 encompasses administering any heparin, and claim 6 limits the heparin to a "biotechnology derived heparin" and that would exclude heparin from porcine mucosa, for example. However, the identical heparin could be both from porcine mucosa

and be biotechnology derived, and since applicants have not defined "biotechnology derived heparin", the claim is not seen to limit that from which it depends.

The rejection of the phrase, "a chemically modified heparin" as being indefinite is maintained for reasons of record. The claim does not set forth how the heparin is modified, and to what extent the heparin is modified. Heparin is an art known compound which can be modified in a multitude of ways. In the absence of the identity of moieties which are intended to modify the art recognized chemical core, described structurally or by chemical name, the identity of "a modified heparin" would be difficult to ascertain. In the absence of said moieties, the claims containing the term "modified" are not described sufficiently to distinctly point out that which applicant intends as the invention. Applicants argue that the term is intended to encompass "heparins that are modified chemically in any of a number of ways, but not such that the chemical core of heparin is unrecognizable". This limitation is not in the claim however. Moreover, applicants argue that the heparins with a recognizable chemical core are known in the art, and point to various references. However, as set forth supra, applicants have not themselves taught as to exactly what a "chemically modified heparin" is. There is absolutely no indication of how heparin is to be modified, with what moieties, in how many locations, or anything of the sort.

The rejection of claim 32 as being indefinite wherein the claim provides that the polysaccharide is optionally a pectin "derivative" is maintained for reasons of record. In the absence of the identity of moieties intended to modify an art recognized chemical core, described structurally or by chemical name, the identity of a "derivative" would be difficult to ascertain. In the absence of said moieties, the claims containing the term "derivative" are not described

particularly sufficiently to distinctly point out that which applicant intends as the invention. Applicants argue that one of ordinary skill in the art would be able to determine a pectin derivative, as the derivatives contain an art recognized core. However, this limitation is not in the claim. One of skill in the art cannot determine the metes and bounds of an undefined term.

The phrase "heparin-like glycosaminoglycan" in every claim which is silent to how the molecule must be like heparin, as in claims 82, 89, and 90, is a relative term which renders the claims indefinite, and therefor the rejection is maintained for reasons of record. The term is not defined by the claims, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. How must another compound be like heparin to be considered "heparin-like"? Must it have the same properties, be the same size, have the same functional groups, comprise the same linking groups? Applicants argue that the term is well known in the art and is defined in the specification on page 20, lines 28-30 as a "family of molecules with heparin like structures and properties". However, this is not seen to be a definition of anything which clearly points out that which applicant is claiming. Applicants additionally note that the claims must be read in light of the specification, and that definitions of terms are not limitations that must be read into the claims. The examiner agrees and has read the claims in light of the specification (which defines "heparin-like" as something which is "heparin-like") and has not read these limitations into the claims.

The rejection of claims 126 and 150 for missing the critical element, as being drawn to compositions including "a polymer to effect slow release of the glycosaminoglycan" is maintained for reasons of record. Claims 140, 199, and 219 are rejected for the same reasons. The claims fail to particularly point out the identity of the polymer to be used in the composition

instantly claimed. The current claim language is drawn to a composition which is not described structurally/formulaically/nomenclatorially; but rather by the various agents' mode of action, function or effect requisite to an activity produced by the composition. The claim is missing the critical element, which is the particular or distinct identity of the polymer to be used in the composition. Defining the polymer structurally, formulaically, or nomenclatorially would be a more preferable way to define the subject matter instead of the current functional description. The claims attempt to limit a composition to additionally include an agent which is defined by its function, i.e., one that effects slow release. Applicants argue that page 16 of the specification defines slow release polymers. However, it is noted that if applicants are relying on the specification for a definition, the specification must clearly set forth the definition explicitly and with reasonably clarity, deliberateness, and precision. See ***Teleflex Inc. v. Ficosa North America Corp., 63 USPQ2d 1374, 1381 (Fed. Cir. 2002); Rexnord Corp. v. Laitram Corp., 60 USPQ2d 1851, 1854 (Fed. Cir. 2001);*** and MPEP 2111.01. It is noted that applicants define their polymers as various molecules "including, but not limited to..." . Exemplification is not seen to be defining something "explicitly and with reasonably clarity, deliberateness, and precision".

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Claim Rejections - 35 USC § 102

The rejection of claims 1-3, 5, 8, 11-12, 14-32, 36-38, 42, 43, 58, 59, 73, 79, 89, 90-91, 99, 113-119, 121-123, 125-126, 130-134, 158-163, 168-170, 176-177, 184-198, and 203 under 35 U.S.C. 102(b) as being anticipated by Illum et al. (WO 97/35562) is maintained for reasons of record. Newly added claims 204-207, 214-216, and 218 are additionally rejected under the same reference.

The claims of the instant application are drawn to various compositions and methods comprising the use of polysaccharides and/or glycosaminoglycans in formulated or unformulated form wherein the polysaccharides are from 1-500 microns in diameter and are delivered into the lung to obtain rapid release. The claims are drawn to various methods of treatment or methods for producing therapeutic effects wherein an unformulated dry polysaccharide particle having a mean geometric diameter of 1-500 microns is administered. The polysaccharides can be low molecular weight heparin, and the disorders treated are any number of various disorders known to be treated by polysaccharides, or various subjects which are at risk of contracting various diseases. It is noted that newly added claims 204-207, 214-216, and 218 all comprise compositions with a diameter of 10-250 microns, and Illum teach of 10 micron compositions as set forth below.

Illum et al. disclose compositions comprising unformulated polysaccharides as microspheres having diameters of 1-10 microns (see above). Moreover, Illum disclose delivering the same to the pulmonary cavity via dry powder devices. The fact that Illum discloses these microspheres and delivering the same to the pulmonary cavity inherently discloses methods of

treatment, and methods of producing therapeutic effects, as the same population are treated with the same compositions, thus the disclosure of Illum is seen to anticipate the methods of treatment as set forth in the instant application.

Illum et al. discloses microspheres which are made from polysaccharides wherein the polysaccharides can be any of amylodextrin, amylopectin, hydroxyethylstarch, carboxymethylcellulose... or polyglucosamine (page 11, lines 25-30). Polyglucosamines are known in the art to be polysaccharides having glucose monomer units with amine functionality in the polysaccharide backbone. Typical polyglucosamines include, for example, chitin, chitosan, and polyglucosaminoglycans which are copolymers of N-acetylglucosamine and various glycan sugars, e.g., hyaluronic acid, chondroitin, heparin, keratan and dermatan (as evidenced by Gruber, US Patent 5,597,811). Illum teaches that their polysaccharide microspheres should be of an aerodynamic diameter of between 1-10 microns (page 13, lines 1-4) and that various modifications may be made to provide for delayed release (i.e., a formulated particle) (page 12, lines 5-11). Illum disclose that their particles can provide rapid release, wherein about 80% of the drug is released just after delivery (within 5 minutes) (page 12, lines 13-17). Claim 6 of Illum discloses low molecular weight heparin as a pharmacological agent in their composition. Illum also discloses that additional agents can be included into their microspheres, such as proteins (page 13). Additionally, since both the instant application and Illum disclose various kits, the kits as claimed in the instant application are seen to be anticipated by Illum as the composition of Illum is disclosed as being useful for pulmonary delivery of agents, wherein any suitable dry powder device may be used for delivery (page 14, lines 7-13).

Illum et al. disclose a polysaccharide system which comprises microspheres of polysaccharides in overlapping size, which are made by a one step process of spray drying a drug and a polysaccharide (the drug can be low molecular weight heparin), thus providing an unformulated polysaccharide. Moreover, Illum disclose alternative embodiments in which the microspheres can be formulated, i.e., for delayed release. Illum disclose their microspheres as being utilized for the pulmonary delivery of drugs wherein a rapid release of the drug is obtained. Illum disclose microspheres having from 1% drug to more than 50% (page 11, lines 1-9). The disclosure of a rapid release (within 5 minutes) is seen to show that the peak concentration would additionally occur rapidly. It is noted, that while Illum is silent to their microspheres' tap density, the examiner believes them to be overlapping with those of the instant application, as the rest of the properties of the compositions are overlapping. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Applicants argue that Illum et al. do not provide a positive teaching that it would be desirable to administer an unformulated dry polysaccharide to produce a therapeutic effect due to the polysaccharide and that the polysaccharides of Illum et al. were carriers, and not the therapeutic agent. However, the examiner would like to note that Illum et al.'s methodological step of administering their polysaccharides would have inherently performed the method as instantly claimed. It is noted that if Illum et al., having taken the manipulative steps described therein, had attempted to measure for the results as described in the instant application, Illum et

al. would have uncovered those results, as they are directly correlative to the method as practiced by Illum et al. Applicant's discovery of differing effects of a prior art method does not give the discoverer a right to exclude others from practicing the prior arts method of administering polysaccharides to produce a therapeutic effects, as the prior arts method would have inherently performed the method as instantly claimed. See ***Ex Parte Novitski, 26 USPQ 2d (BNA) 1389.*** A hypothetical example clarifies this principle. Humans lit fires for thousands of years before realizing that oxygen is necessary to create and maintain a flame. The first person to discover the necessity of oxygen certainly could not have obtained a valid patent claim for "a method of making a fire by lighting a flame in the presence of oxygen." Even if prior art on lighting fires did not disclose the importance of oxygen and one of ordinary skill in the art did not know about the importance of oxygen, understanding this law of nature would not give the discoverer a right to exclude others from practicing the prior art of making fires. ***EMI v. Cypress Semiconductor,*** **2001 US Fed. Cir. Ct. of App.** In the instant case, applicant's arguments that Illum et al. is silent to the polysaccharide producing the therapeutic effect is not convincing, as their polysaccharides must have produced a therapeutic effect. Applicants additionally argue that Illum does not directly provide for their specific polysaccharides in dry form other than in the long list of drugs which can be encapsulated. However, Illum claim various agents which can be included in their compositions, see claims 4-17 for example. Applicants additionally argue that Illum do not teach of polysaccharides of less than 10 microns. It is noted that none of the claims with a range outside of 10 microns has been rejected under the Illum reference.

Claims 4, 13, 33-35, 127-129, 135-139, 164-167, 200-202, 208-213, 217-218, and 220-222 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
February 22, 2005

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623